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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,759	ZHOU, MINGDONG	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *5 and 15-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 December 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed September 5, 2008 in response to the Office Action of June 11, 2008 is acknowledged. Applicant elected without traverse Group I, claims 1-14, and the species of protein or peptide "amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14" and species of neoplasm "breast cancer."

Claims 1-43 are pending. Claim 5 is amended and is withdrawn as being drawn to a non-elected species. Claims 15-43 are withdrawn from further consideration by the examiner under 35 CFR 1.142(b) as being drawn to non-elected inventions. Claims 1-4 and 6-14 are currently being examined.

Specification/ Drawings

2. The drawing and specification are objected to. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.8821 (a)(1) and (a)(2). Specifically, there is **no SEQ ID NO identified with the nucleotide sequence disclosed in Figure 23.** 37 CFR 1.821(d) requires that a reference to a particular sequence identifier (i.e., SEQ ID NO:#) be made in the specification and claims wherever a reference is made to that sequence (See MPEP 2422.02). Applicants may obviate this objection by amending the Brief Description of the Drawings or the Drawings to identify the nucleotide sequence.

If Applicants choose to amend the Drawings: any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an

amended drawing should not be labeled as "amended." Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-3 and 6-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The claims are drawn to a method for preventing, treating or delaying neoplasm in a mammal, comprising administering to a mammal an amount of **an ErbB-3 protein, or functional fragment thereof,** whereby an immune response is generated against said neoplasm and said neoplasm is prevented, treated, or delayed (claims 1, 2, 6, 12, 13, 14), the method of claim 1, wherein an amount of **an extracellular domain of an ErbB-3 protein, or a functional fragment thereof** is administered (claim 3), the method of claim 1 wherein the **ErbB-3 protein, or a functional fragment thereof**, is

administered to the neoplasm *in situ* (claim 7), the method of claim 1 wherein the **ErbB-3 protein or a functional fragment thereof** is co-administered with a pharmaceutically acceptable carrier (claim 9), the method of claim 1 wherein the **ErbB-3 protein or a functional fragment thereof** is co-administered with an anti-neoplastic agent (claim 10, 11).

The specification discloses that any suitable ErbB-3 protein or functional fragment thereof that can elicit an immune response to the neoplasm can be used in the present method. The specification discloses that ErbB-3 proteins or fragments disclosed in US Patent 5,820,859 can be used, or those derived from rat ErbB-3, from puffer fish ErbB-3, or derived from human ErbB-3 (p. 12, section B). The specification discloses that SEQ ID NO:14 is the ErbB-3 extracellular domain of ErbB-3 (p. 25) and the protein, SEQ ID NO:14, also named rhErbB3-f12, was used to inoculate mice. It appears rhErbB3-f12 delayed tumor growth or reduced tumor growth in inoculated mice compared to controls, however the type of cancer the mice developed is unclear (i.e., breast, lung, etc) (Table 4, p. 30). The specification does not disclose any other ErbB-3 proteins, extracellular domains, or functional fragments thereof as broadly encompassed in the claims.

The art (see US Patent 5,183,884, Kraus et al) teaches the sequence of human ErbB-3, and Lee et al (Cancer Research, 2001, 61:4467-4473) teach the extracellular domain of ErbB-3 that is amino acids 1-620 (Figure 1), however these sequences do not provide an adequate representative number of species to support adequate written

description for the broad genus of ErbB-3 proteins, extracellular domains, and functional fragments thereof as encompassed by the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a recitation of "an ErbB-3 protein, or functional fragment thereof," or "an extracellular domain of an ErbB-3 protein, or a functional fragment thereof". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because

> it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed

correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of ErbB-3 proteins, extracellular domains, and functional fragments thereof, per Lilly by structurally describing representative ErbB-3 proteins, extracellular domains, and functional fragments thereof or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe ErbB-3 proteins, extracellular domains, and functional fragments thereof useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. Although the specification discloses human, rat, and puffer fish ErbB-3 proteins as well as extracellular domain fragment SEQ ID NO:14, this does not provide a description of the broadly claimed ErbB-3 proteins, extracellular domains, and functional fragments thereof that would

satisfy the standard set out in Enzo because the specification provides no structural features coupled to functional characteristics.

Further, the specification also fails to describe ErbB-3 proteins, extracellular domains, and functional fragments by the test set out in Lilly because the specification describes only human, rat, and puffer fish ErbB-3 proteins as well as extracellular domain fragment SEQ ID NO:14. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of ErbB-3 proteins, extracellular domains, and functional fragments that is required to practice the claimed invention. Since the specification fails to adequately describe the product to which the claimed method uses, it also fails to adequately describe the method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4, 6, 7, and 9-14 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/02540, Fizpatrick et al, published 1/22/1998.

It is noted the instant specification defines *"in situ"* administration to a neoplasm as administration to the place where the neoplasm is located or the vicinity thereof (p. 14).

The claims are drawn to a method for preventing, treating or delaying neoplasm in a mammal, which method comprises administering to a mammal, to which such prevention, treatment or delay is needed or desirable, an effective amount of an ErbB-3 protein, or a functional fragment thereof, whereby an immune response is generated against said neoplasm and said neoplasm is prevented, treated or delayed (claim 1), the method of claim 1, wherein the mammal is a human (claim 2), the method of claim 1, wherein an effective amount of an extracellular domain of an ErbB-3 protein is administered (claim 3), the method of claim 1, wherein the ErbB-3 protein comprises at least amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO: 14 (claim 4), the method of claim 1, further comprising administering an immune response potentiator to the mammal (claim 6), wherein the ErbB-3 protein, or a functional fragment thereof, is administered to the neoplasm *in situ* (claim 7), the method of claim 1, wherein the ErbB-3 protein, or a functional fragment thereof, is co-administered with a pharmaceutically acceptable carrier or excipient (claim 9), the method of claim 1, wherein the ErbB-3 protein, or a functional fragment thereof, is co-administered with an anti-neoplasm agent (claim 10), the method of claim 10, wherein the anti-neoplasm agent is selected from the group consisting of an anti-angiogenic agent, a natural product, an antagonist, an oncogene inhibitor, an anti-oncogene antibody (claim 11), the method of claim 1, wherein the neoplasm to be prevented, treated or delayed is breast cancer (12-14).

Fizpatrick et al teach a method for treating or preventing a neoplasm in a mammal comprising administering to the mammal, the extracellular domain protein of

human ErbB-3 (p. 8, line 38 through p. 9, line 12; p. 9, lines 32 through p. 10, line 3; p. 19, lines 31-33; p. 27, lines 8-9; Examples 2-3; claims 7, 37, 38), wherein the neoplasm is breast cancer (p. 15, line 10; p. 25, lines 1-10), wherein the mammal is human (p. 19, lines 34-36), wherein the ErbB-3 protein is administered in a pharmaceutically acceptable carrier or excipient (p. 19, lines 37 to p. 20, line 2; p. 26, lines 3-14), wherein the ErbB-3 protein is administered with an immune response potentiator or adjuvant such as a cytokine (p. 27, lines 19-20), wherein the ErbB-3 protein is co-administered with an antineoplastic agent which includes anti-angiogenic agents and antibody antagonists of oncogene growth receptors (p. 27, 10-20), wherein the ErbB-3 protein is administered by intravenous, intraperitoneal, intraarterial, all of which would be injection in the vicinity of the neoplasm (p. 26, lines 22-25), and wherein the ErbB-3 protein comprises the N-terminal 636 amino acids (p. 35, line 25), which includes the extracellular domain hence, necessarily comprises at least amino acid residues 24-81 of SEQ ID NO:14 of the instant application (residues 24-81 are the equivalent of residues 483-540 of ErbB-3). Given Fizpatrick et al teach a method for treating or preventing a neoplasm in a mammal comprising the same claimed step of administering to the mammal the extracellular domain protein of human ErbB-3, the method taught by Fizpatrick et al would generate an immune response against said neoplasm.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/02540, Fizpatrick et al, published 1/22/1998.

It is noted the instant specification defines *"in situ"* administration to a neoplasm as administration to the place where the neoplasm is located or the vicinity thereof (p. 14).

The claims are drawn to a method for preventing, treating or delaying neoplasm in a mammal, which method comprises administering to a mammal, to which such prevention, treatment or delay is needed or desirable, an effective amount of an ErbB-3 protein, or a functional fragment thereof, whereby an immune response is generated against said neoplasm and said neoplasm is prevented, treated or delayed (claim 1), wherein the ErbB-3 protein, or a functional fragment thereof, is administered to the neoplasm *in situ* (claim 7), the method of claim 7, further comprising administering an immune response potentiator to the neoplasm *in situ* (claim 8).

Fizpatrick et al teach a method for treating or preventing a neoplasm in a mammal comprising administering to the mammal, the extracellular domain protein of human ErbB-3 (p. 8, line 38 through p. 9, line 12; p. 9, lines 32 through p. 10, line 3; p. 19, lines 31-33; p. 27, lines 8-9; Examples 2-3; claims 7, 37, 38), wherein the neoplasm is breast cancer (p. 15, line 10; p. 25, lines 1-10), wherein the ErbB-3 protein is administered with an immune response potentiator or adjuvant such as a cytokine (p. 27, lines 19-20), as set forth above. Given Fizpatrick et al teach a method for treating or

preventing a neoplasm in a mammal comprising the same claimed step of administering to the mammal, the extracellular domain protein of human ErbB-3, the method taught by Fizpatrick et al would generate an immune response against said neoplasm. Fizpatrick et al further teach administration routes by intravenous, intraperitoneal, intraarterial, all of which would be injection in the vicinity of the neoplasm (p. 26, lines 22-25) and that the route of administration may be modified to obtain a maximum therapeutic effect (p. 27, lines 21-26). Fizpatrick et al teach that it is desirable to treat a mammal with the ErbB-3 protein where excessive levels of heregulin ligand are present or excessive activation of receptors by heregulin is occurring in the mammal, including breast cancer (p. 25, lines 1-4).

Fizpatrick et al does not teach administration of the ErbB-3 protein or immune response potentiator the neoplasm *in situ* by means of directly to the tumor.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer the ErbB-3 protein or immune response potentiator the to the neoplasm because Fizpatrick et al teach that the route of administration may be modified to obtain a maximum therapeutic effect and treatment at the site where excessive levels of heregulin ligand are present or excessive activation of receptors by heregulin is occurring in the mammal, such as cancer, is desirable. One would have been motivated to administer the ErbB-3 protein or immune response potentiator to the neoplasm in order to treat the neoplasm. One of ordinary skill in the art would have a reasonable expectation of success administering the ErbB-3 protein or

immune response potentiator to the neoplasm because methods of administering proteins to or in the vicinity of a neoplasm are known and successful in the art.

6. **Conclusion:** No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Examiner, Art Unit 1642